PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:
AMY E. MANDRAGOURAS
LAHIVE & COCKFIELD, LLP
28 STATE STREET
BOSTON, MA 02109

PCT

NOTIFICATION OF TRANSMITTAL OF INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Rule 71.1)

Date of Mailing *(day/month/year)*	23 MAR 2001
Applicant's or agent's file reference DFN-031PC	**IMPORTANT NOTIFICATION**

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/US99/25439	29 October 1999 (29.10.1999)	29 October 1998 (29.10.1998)

Applicant

DANA-FARBER CANCER INSTITUTE, INC.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.

2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.

3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices)(Article 39(1))(see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703)305-3230	Authorized officer Ulrike Winkler, Ph.D. Telephone No. 703-308-0196

Form PCT/IPEA/416 (July 1992)

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference DFN-031PC	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/US99/25439	International filing date *(day/month/year)* 29 October 1999 (29.10.1999)	Priority date *(day/month/year)* 29 October 1998 (29.10.1998)
International Patent Classification (IPC) or national classification and IPC IPC(7): C07K 1/00 and US Cl.: 530/350		
Applicant DANA-FARBER CANCER INSTITUTE, INC.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 2 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of ___ sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☐ Non-establishment of report with regard to novelty, inventive step and industrial applicability
   - IV ☒ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☒ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
26 May 2000 (26.05.2000)	20 February 2001 (20.02.2001)
Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703)305-3230	Authorized officer Ulrike Winkler, Ph.D. Telephone No. 703-308-0196

Form PCT/IPEA/409 (cover sheet)(July 1998)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US25439

I. Basis of the report

1. With regard to the **elements** of the international application:*

☒ the international application as originally filed.

☒ the description:
pages 1-94 as originally filed
pages NONE , filed with the demand
pages NONE , filed with the letter of _____.

☒ the claims:
pages 95-99 , as originally filed
pages NONE , as amended (together with any statement) under Article 19
pages NONE , filed with the demand
pages NONE , filed with the letter of _____.

☒ the drawings:
pages 1-23 , as originally filed
pages NONE , filed with the demand
pages NONE , filed with the letter of _____.

☒ the sequence listing part of the description:
pages 1-25 , as originally filed
pages NONE , filed with the demand
pages NONE , filed with the letter of _____.

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language _____ which is:

☐ the language of a translation furnished for the purposes of international search (under Rule23.1(b)).

☐ the language of publication of the international application (under Rule 48.3(b)).

☐ the language of the translation furnished for the purposes of international preliminary examination(under Rules 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

☒ contained in the international application in printed form.

☒ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☒ The amendments have resulted in the cancellation of:

☒ the description, pages NONE

☒ the claims, Nos. NONE

☒ the drawings, sheets/~~fig~~ NONE

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

** Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).*

*** Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.*

IV. Lack of unity of invention

1. In response to the invitation to restrict or pay additional fees the applicant has:

☒ restricted the claims.

☐ paid additional fees.

☐ paid additional fees under protest.

☐ neither restricted nor paid additional fees.

2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention is accordance with Rules 13.1, 13.2 and 13.3 is

☐ complied with.

☒ not complied with for the following reasons:

Please See Continuation Sheet

4. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this report:

☐ all parts.

☒ the parts relating to claims Nos. 1-10

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. STATEMENT

Novelty (N)	Claims	1-3 and 6-10	YES
	Claims	4 and 5	NO
Inventive Step (IS)	Claims	1-3	YES
	Claims	4-10	NO
Industrial Applicability (IA)	Claims	1-10	YES
	Claims	NONE	NO

2. CITATIONS AND EXPLANATIONS (Rule 70.7)
Please See Continuation Sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the questions whether the claims are fully supported by the description, are made:

Claim 5 is objected to under PCT Rule 66.2(a)(v) as lacking clarity under PCT Article 6 because claim 5 is indefinite for the following reason(s): It is not clear how large the hybridizing nucleic acid molecule needs to be to qualify as hybridizing under stringent conditions.

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of Certain Documents Cited

1. Certain published documents (Rule 70.10)

Application No Patent No.	Publication Date *(day/month/year)*	Filing Date *(day/month/year)*	Priority date (valid claim) *(day/month/year)*
None	None	None	None

2. Non-written disclosures (Rule 70.9)

Kind of non-written disclosure	Date of non-written disclosure *(day/month/year)*	Date of written disclosure referring to non-written disclosure *(day/month/year)*
None	None	None

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

IV. 3. This Authority considers that the requirement of unity of invention is accordance with Rules 13.1, 13.2 and 13.3 is not complied with for the following reasons:
This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I, claim(s) 1-10, drawn to isolated nucleic acids, a vector containing the isolated nucleic acid and a method of producing the polypeptide encoded by the nucleic acid.

Group II, claim(s) 11-13, drawn to isolated polypeptides.

Group III, claim(s) 14, drawn to an antibody.

Group IV, claim(s) 15-17, drawn to a method of detecting the polypeptide and assembling a kit to detect the polypeptide.

Group V, claim(s) 18-20, drawn to a method of detecting nucleic acids an assembling a kit to detect nucleic acids.

Group VI, claim(s) 21-24, drawn to a method of identifying a compound that binds the polypeptide.

The inventions listed as Groups I-VI do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

The special technical feature of group I is the nucleic acid which is used in an expression vector system.
The special technical feature of group II is the isolated polypeptide.
The special technical feature of group III is the antibody directed to the polypeptide.
The special technical feature of group IV is a method of detecting the polypeptide using the antibody.
The special technical feature of group V is a nucleic acid primer or probe used to detect the nucleic acid.
The special technical feature of group VI is a method of identifying compounds that bind the polypeptide

Groups I-III are compositions and are distinct from groups IV-VI which are drawn to methods. Groups I-III are compositions and each is distinct from the other because they contain different materials. Group I comprises the DNA sequence for the protein; and DNA is made up of nucleic acids. Additionally, Group I contains an expression vector, and a transformed host cells as well as a method of producing a polypeptide from the nucleic acid. Group II comprises an isolated and purified protein and proteins are made up of amino acids. Group III comprises an antibody to the protein, although antibodies themselves are proteins, they are different molecules with different structures.

Groups IV-VI are drawn to methods and each is distinct from the other because they utilize different starting materials, therefore the outcomes are not be expected to be the same. Groups IV are drawn to a method detecting the polypeptide using an antibody. Group V is a method for detecting nucleic acids using nucleic acid primers and probes. Group VI is a method for identifying compounds that bind the polypeptide. The method of Group VI uses different steps from the other methods, thereby setting it apart.

Accordingly, Groups I-VI are not so linked by the same or corresponding technical feature as to form a single inventive concept.

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

V. 2. Citations and Explanations:

Claims 4 and 5 lack novelty under PCT Article 33(2) as being anticipated by Banaldo et al. (Genome Research 1996). The instant invention is drawn to isolated nucleic acids selected from the group consisting of SEQ ID NO: 1, 2, 3 or 4, specifically a fragment that is at least 607 amino acids in length, or fragments that correspond to at least 15 contiguous amino acids of SEQ ID NO: 2 or 5. In addition, the claimed invention includes isolated nucleic acid molecules which hybridize to SEQ ID NO: 1, 2, 3 or 4. Banaldo et al. disclose an expressed sequence tag representing 620 nucleic acids of SEQ ID NO: 4, additionally this fragment encodes at least 15 contiguous amino acid residues of SEQ ID NO: 5. Therefore, the instant invention is anticipated by Banaldo et al.

Claims 4 and 5 lack novelty under PCT Article 33(2) as being anticipated by Zambrowicz et al. (Nature 1998). The instant invention is drawn to isolated nucleic acids selected from the group consisting of SEQ ID NO: 1, 2, 3 or 4, specifically that correspond to at least 15 contiguous amino acids of SEQ ID NO: 2 or 5. In addition, the claimed invention includes isolated nucleic acid molecules which hybridize to SEQ ID NO: 1, 2, 3 or 4. Zambrowicz et al. disclose an expressed sequence tag representing SEQ ID NO: 4, which encodes at least 15 contiguous amino acid residues of SEQ ID NO:5. Therefore, the instant invention is anticipated by Zambrowicz et al.

Claims 4 and 5 lack novelty under PCT Article 33(2) as being anticipated by Adams et al. (Nature Genetics 1993). The instant invention is drawn to isolated nucleic acids selected from the group consisting of SEQ ID NO: 1, 2, 3 or 4, specifically that correspond to at least 15 contiguous amino acids of SEQ ID NO: 2 or 5. In addition the claimed invention includes isolated nucleic acid molecules which hybridize to SEQ ID NO: 1, 2, 3 or 4. Adams et al. disclose an expressed sequence tag representing SEQ ID NO: 3, which encodes at least 15 contiguous amino acid residues of SEQ ID NO:2. Therefore, the instant invention is anticipated by Adams et al.

Claims 4 -10 lack an inventive step under PCT Article 33(3) as being obvious over Banaldo et al. (Genome Research 1996), Zambrowicz et al. (Nature 1998) or Adams et al. (Nature Genetics 1993) each in view of the Pharmacia Catalog (1996). The instant invention is drawn an isolated nucleic acid comprising at least 607 nucleotides selected from the group consisting of SEQ ID NO: 1, 2, 3 or 4 or corresponding to at least 15 contiguous amino acids of SEQ ID NO: 2 or 5. The relevance of Banaldo et al., Zambrowicz et al. and Adams et al. has been discussed above. The references do not teach inserting the nucleic acid segments into an expression vector. Expressing polypeptides or fragments of polypeptides using an expression vector system including GST fusion protein expression systems is notoriously well established in the art as indicated by the commercially available expression systems indicated in the Pharmacia Catalog. One of ordinary skill in the art would be motivated express these nucleic acids in order to use them antigens for the production of antibodies. Therefore, the instant invention is obvious over Banaldo et al., Zambrowicz et al. or Adams et al. each in view of the Pharmacia Catalog.

Claims 1-3 meet the criteria set out in PCT Article 33 (2) and (3), because the prior art does not teach or fairly suggest the isolation and purification of nucleic acids comprising the entire sequence of SEQ ID NO: 1, 2, 3 or 4. The prior art additionally does not disclose nucleic acids encoding the entire polypeptide comprising SEQ ID NO: 2 and 5. The prior art discloses expressed sequence tags that contain a portion of the nucleic acid sequences set out in SEQ ID NO: 3, 4 or 6. There is no indication in the prior art that would have led the ordinary artisan to sequence the entire nucleic acid. Therefore, the subject matter of claims 1-3 is novel and inventive as required by PCT Article 33 (2) and (3).

Claims 1-10 meet the criteria of industrial applicability set out in PCT Article 33 (4).

---------- NEW CITATIONS ----------

PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:
AMY E. MANDRAGOURAS
LAHIVE & COCKFIELD, LLP
28 STATE STREET
BOSTON, MA 02109

NOV 29, 2000 - 5 DAY NOTICE
DEC 4, 2000 - WRITTEN OPINION

PCT

WRITTEN OPINION

(PCT Rule 66)

Date of Mailing *(day/month/year)*	04 OCT 2000
Applicant's or agent's file reference DFN-031PC	REPLY DUE within 2 months/days from the above date of mailing

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/US99/25439	29 October 1999 (29.10.1999)	29 October 1998 (29.10.1998)

International Patent Classification (IPC) or both national classification and IPC

IPC(7): C07K 1/00 and US Cl.: 530/350

Applicant

DANA-FARBER CANCER INSTITUTE, INC.

1. This written opinion is the first (first, etc,) drawn by this International Preliminary Examining Authority.

2. This opinion contains indications relating to the following items:

I	☒	Basis of the opinion
II	☐	Priority
III	☐	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
IV	☒	Lack of unity of invention
V	☒	Reasoned statement under Rule 66.2 (a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
VI	☐	Certain documents cited
VII	☐	Certain defects in the international application
VIII	☒	Certain observations on the international application

3. The applicant is hereby **invited to reply** to this opinion.

When? See the time limit indicated above. ~~The applicant may, before the expiration of that time limit, request this Authority to grant an extension. See rule 66.2(d).~~

How? By submitting a written reply, accompanied, where appropriate, by amendments, according to Rule 66.3. For the form and the language of the amendments, see Rules 66.8 and 66.9.

Also For an additional opportunity to submit amendments, see Rule 66.4.
For the examiner's obligation to consider amendments and/or arguments, see Rule 66.4 *bis*.
For an informal communication with the examiner, see Rule 66.6

If no reply is filed, the international preliminary examination report will be established on the basis of this opinion.

4. The final date by which the international preliminary examination report must be established according to Rule 69.2 is: 28 February 2001 (28.02.2001)

Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer Ulrike Winkler, Ph.D. Telephone No. 703-308-0196

Form PCT/IPEA/408 (cover sheet)(July 1998)

WRITTEN OPINION

Internal application No.
PCT/US99/25439

I. Basis of the opinion

1. With regard to the **elements** of the international application:*

☒ the international application as originally filed

☒ the description:
pages 1-94, as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.

☒ the claims:
pages 95-99, as originally filed
pages NONE, as amended (together with any statement) under Article 19
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.

☒ the drawings:
pages 1-23, as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.

☒ the sequence listing part of the description:
pages 1-25, as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language _____ which is:

☐ the language of a translation furnished for the purposes of international search (under Rule23.1(b)).

☐ the language of publication of the international application (under Rule 48.3(b)).

☐ the language of the translation furnished for the purposes of international preliminary examination(under Rules 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the written opinion was drawn on the basis of the sequence listing:

☒ contained in the international application in printed form.

☒ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☒ The amendments have resulted in the cancellation of:

☒ the description, pages NONE

☒ the claims, Nos. NONE

☒ the drawings, sheets~~/fig~~ NONE

5. ☐ This opinion has been drawn as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

** Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this opinion as "originally filed."*

WRITTEN OPINION

Internat[redacted]application No.
PCT/US99/25439

IV. Lack of unity of invention

1. In response to the invitation (Form PCT/IPEA/405) to restrict or pay additional fees the applicant has:

- [x] restricted the claims.
- [ ] paid additional fees.
- [ ] paid additional fees under protest.
- [ ] neither restricted nor paid additional fees.

2. This Authority found that the requirement of unity of invention is not complied with for the following reasons and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees:

3. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this opinion:

- [ ] all parts.
- [x] the parts relating to claims Nos. 1-10.

WRITTEN OPINION

International application No.
PCT/US99/25439

V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. STATEMENT

Novelty (N)	Claims	1-3 and 6-10	YES
	Claims	4 and 5	NO
Inventive Step (IS)	Claims	1-3	YES
	Claims	4-10	NO
Industrial Applicability (IA)	Claims	1-10	YES
	Claims	NONE	NO

2. CITATIONS AND EXPLANATIONS

Please See Continuation Sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the questions whether the claims are fully supported by the description, are made:

Claim 5 is objected to under PCT Rule 66.2(a)(v) as lacking clarity under PCT Article 6 because claim 5 is indefinite for the following reason(s): It is not clear how large the hybridizing nucleic acid molecule needs to be to qualify as hybridizing under stringent conditions.

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

TIME LIMIT:
The time limit set for response to a Written Opinion may not be extended. 37 CFR 1.484(d). Any response received after the expiration of the time limit set in the Written Opinion will not be considered in preparing the International Preliminary Examination Report.

V. 2. Citations and Explanations:
Claims 4 and 5 lack novelty under PCT Article 33(2) as being anticipated by Banaldo et al. (Genome Research 1996). The instant invention is drawn to isolated nucleic acids selected from the group consisting of SEQ ID NO: 1, 2, 3 or 4, specifically a fragment that is at least 607 amino acids in length, or fragments that correspond to at least 15 contiguous amino acids of SEQ ID NO: 2 or 5. In addition, the claimed invention includes isolated nucleic acid molecules which hybridize to SEQ ID NO: 1, 2, 3 or 4. Banaldo et al. disclose an expressed sequence tag representing 620 nucleic acids of SEQ ID NO: 4, additionally this fragment encodes at least 15 contiguous amino acid residues of SEQ ID NO: 5. Therefore, the instant invention is anticipated by Banaldo et al.

Claims 4 and 5 lack novelty under PCT Article 33(2) as being anticipated by Zambrowicz et al. (Nature 1998). The instant invention is drawn to isolated nucleic acids selected from the group consisting of SEQ ID NO: 1, 2, 3 or 4, specifically that correspond to at least 15 contiguous amino acids of SEQ ID NO: 2 or 5. In addition, the claimed invention includes isolated nucleic acid molecules which hybridize to SEQ ID NO: 1, 2, 3 or 4. Zambrowicz et al. disclose an expressed sequence tag representing SEQ ID NO: 4, which encodes at least 15 contiguous amino acid residues of SEQ ID NO:5. Therefore, the instant invention is anticipated by Zambrowicz et al.

Claims 4 and 5 lack novelty under PCT Article 33(2) as being anticipated by Adams et al. (Nature Genetics 1993). The instant invention is drawn to isolated nucleic acids selected from the group consisting of SEQ ID NO: 1, 2, 3 or 4, specifically that correspond to at least 15 contiguous amino acids of SEQ ID NO: 2 or 5. In addition the claimed invention includes isolated nucleic acid molecules which hybridize to SEQ ID NO: 1, 2, 3 or 4. Adams et al. disclose an expressed sequence tag representing SEQ ID NO: 3, which encodes at least 15 contiguous amino acid residues of SEQ ID NO:2. Therefore, the instant invention is anticipated by Adams et al.

Claims 4 -10 lack an inventive step under PCT Article 33(3) as being obvious over Banaldo et al. (Genome Research 1996), Zambrowicz et al. (Nature 1998) or Adams et al. (Nature Genetics 1993) each in view of the Pharmacia Catalog (1996). The instant invention is drawn an isolated nucleic acid comprising at least 607 nucleotides selected from the group consisting of SEQ ID NO: 1, 2, 3 or 4 or corresponding to at least 15 contiguous amino acids of SEQ ID NO: 2 or 5. The relevance of Banaldo et al., Zambrowicz et al. and Adams et al. has been discussed above. The references do not teach inserting the nucleic acid segments into an expression vector. Expressing polypeptides or fragments of polypeptides using an expression vector system including GST fusion protein expression systems is notoriously well established in the art as indicated by the commercially available expression systems indicated in the Pharmacia Catalog. One of ordinary skill in the art would be motivated express these nucleic acids in order to use them antigens for the production of antibodies. Therefore, the instant invention is obvious over Banaldo et al., Zambrowicz et al. or Adams et al. each in view of the Pharmacia Catalog.

Claims 1-3 meet the criteria set out in PCT Article 33 (2) and (3), because the prior art does not teach or fairly suggest the isolation and purification of nucleic acids comprising the entire sequence of SEQ ID NO: 1, 2, 3 or 4. The prior art additionally does not disclose nucleic acids encoding the entire polypeptide comprising SEQ ID NO: 2 and 5. The prior art discloses expressed sequence tags that contain a portion of the nucleic acid sequences set out in SEQ ID NO: 3, 4 or 6. There is no indication in the prior art that would have led the ordinary artisan to sequence the entire nucleic acid. Therefore, the subject matter of claims 1-3 is novel and inventive as required by PCT Article 33 (2) and (3).

CHAPTER II
PCT TELEPHONE MEMORANDUM
FOR
LACK OF UNITY OF INVENTION

PCT No.: PCT/US99/25439

Examiner: Ulrike Winkler, Ph.D.

Attorney spoken to: Maria Laccotripe

Date of call: 03 August 2000

☐ Amount of payment approved:

☐ Deposit account number to be charged:

☐ Attorney elected to pay for ALL additional inventions

☐ Attorney elected to pay only for the additional inventions covered by

☐ Group(s):

-- encompassing --

☐ Claim(s):

☒ Attorney elected NOT to pay for any additional inventions, therefore, only the first claimed invention Grou I, covered by Claim(s) 1-10 has been examined.

☒ Attorney was orally advised that there is no right to protest for any group not paid for.

☒ Attorney was orally advised that any protest must be filed no later than 1 Month from the mailing of the Opinion (Form PCT/IPEA/408) or the Final Report (Form PCT/IPEA/409).

Time Limit For Filing A Protest

Applicant is hereby given 1 Month from the mailing date of this Opinion/Final Report in which to file a protest of the holding of lack of unity of invention. In accordance with PCT Rule 68.3, applicant may protest the holding of lack of unity only with respect to the group(s) paid for.

Itemized Summary of Claim Groupings:
Please See Continuation Sheet

Detailed Reasons For Holding Lack of Unity of Invention:
Please See Continuation Sheet

Note: A copy of this form must be attached to the Opinion/Final Report.

ATTACHMENT TO CHAPTER II PCT TELEPHONE MEMORANDUM FOR LACK OF UNITY OF INVENTION

Itemized Summary of Claim Groupings:

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I, claim(s) 1-10, drawn to isolated nucleic acids, a vector containing the isolated nucleic acid and a method of producing the polypeptide encoded by the nucleic acid.

Group II, claim(s) 11-13, drawn to isolated polypeptides.

Group III, claim(s) 14, drawn to an antibody.

Group IV, claim(s) 15-17, drawn to a method of detecting the polypeptide and assembling a kit to detect the polypeptide.

Group V, claim(s) 18-20, drawn to a method of detecting nucleic acids an assembling a kit to detect nucleic acids.

Group VI, claim(s) 21-24, drawn to a method of identifying a compound that binds the polypeptide.

Detailed Reasons For Holding Lack of Unity of Invention:

The inventions listed as Groups I-VI do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

The special technical feature of group I is the nucleic acid which is used in an expression vector system.
The special technical feature of group II is the isolated polypeptide.
The special technical feature of group III is the antibody directed to the polypeptide.
The special technical feature of group IV is a method of detecting the polypeptide using the antibody.
The special technical feature of group V is a nucleic acid primer or probe used to detect the nucleic acid.
The special technical feature of group VI is a method of identifying compounds that bind the polypeptide

Groups I-III are compositions and are distinct from groups IV-VI which are drawn to methods. Groups I-III are compositions and each is distinct from the other because they contain different materials. Group I comprises the DNA sequence for the protein; and DNA is made up of nucleic acids. Additionally, Group I contains an expression vector, and a transformed host cells as well as a method of producing a polypeptide from the nucleic acid. Group II comprises an isolated and purified protein and proteins are made up of amino acids. Group III comprises an antibody to the protein, although antibodies themselves are proteins, they are different molecules with different structures.

Groups IV-VI are drawn to methods and each is distinct from the other because they utilize different starting materials, therefore the outcomes are not be expected to be the same. Groups IV are drawn to a method detecting the polypeptide using an antibody. Group V is a method for detecting nucleic acids using nucleic acid primers and probes. Group VI is a method for identifying compounds that bind the polypeptide. The method of Group VI uses different steps from the other methods, thereby setting it apart.

Accordingly, Groups I-VI are not so linked by the same or corresponding technical feature as to form a single inventive concept.

Note: A copy of this form must be attached to the Opinion/Final Report.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US99/25439

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : C07K 1/00
US CL : 530/350

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
U.S. : 530/350

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
Please See Continuation Sheet

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	ADAMS et al. Rapid cDNA sequencing (expressed sequence tags) from a directionally cloned human infant brain cDNA library. Nature Genetics. August 1993, Vol. 4, No. 4, pages 373-380, (ABSTACT only).	1,4,5
X	BONALDO et al. Normalization and subtraction:two approaches to facilitate gene discovery. Genome Research. September 1996, Vol. 6, No. 9, pages 791-806, (ABSTRACT only).	1,4,5
X	ZAMBROWICZ et al. Disruption and sequence identification of 2000 genes in mouse embryonic stem cells. Nature. 09 April 1998, Vol. 392, pages 608-611, see entire document.	1,4,5
Y	PHARMACIA Overview of molecular biology products. Pharmacia Biotech. 1996, pages 107, 110-117, 139, 163-165.	5, 7-9, 18
A		10, 19, 20
Y	MERCER D.W. Immunoassays for the detection of tumor associated antigens. In: Manual of clinical laboratory immunology. Edited by: Rose et al., Washington D.C., American Society for Microbiology, 4th Ed, pages 791-795	14-17, 21-24

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
15 February 2000 (15.02.2000)	02 MAR 2000
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer Ulrike Winkler, Ph.D. Telephone No. 703-308-0196

Form PCT/ISA/210 (second sheet) (July 1998)

Continuation of B. FIELDS **SEARCHED Item 3:** Medline, STIC
B cell aggressive lymphoma, antibody, Elisa,

PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTICE INFORMING THE APPLICANT OF THE COMMUNICATION OF THE INTERNATIONAL APPLICATION TO THE DESIGNATED OFFICES

(PCT Rule 47.1(c), first sentence)

To:
MANDRAGOURAS, Amy, E.
Lahive & Cockfield, LLP
28 State Street
Boston, MA 02109
ETATS-UNIS D'AMERIQUE

Date of mailing (day/month/year) 11 May 2000 (11.05.00)		
Applicant's or agent's file reference DFN-031PC	**IMPORTANT NOTICE**	
International application No. PCT/US99/25439	**International filing date** (day/month/year) 29 October 1999 (29.10.99)	**Priority date** (day/month/year) 29 October 1998 (29.10.98)
Applicant DANA-FARBER CANCER INSTITUTE et al		

1. Notice is hereby given that the International Bureau has communicated, as provided in Article 20, the international application to the following designated Offices on the date indicated above as the date of mailing of this Notice:
   JP,US

   In accordance with Rule 47.1(c), third sentence, those Offices will accept the present Notice as conclusive evidence that the communication of the international application has duly taken place on the date of mailing indicated above and no copy of the international application is required to be furnished by the applicant to the designated Office(s).

2. The following designated Offices have waived the requirement for such a communication at this time:
   CA,EP

   The communication will be made to those Offices only upon their request. Furthermore, those Offices do not require the applicant to furnish a copy of the international application (Rule 49.1(a-bis)).

3. Enclosed with this Notice is a copy of the international application as published by the International Bureau on
   11 May 2000 (11.05.00) under No. WO 00/26231

REMINDER REGARDING CHAPTER II (Article 31(2)(a) and Rule 54.2)

If the applicant wishes to postpone entry into the national phase until 30 months (or later in some Offices) from the priority date, **a demand for international preliminary examination** must be filed with the competent International Preliminary Examining Authority before the expiration of 19 months from the priority date.

It is the applicant's sole responsibility to monitor the 19-month time limit.

Note that only an applicant who is a national or resident of a PCT Contracting State which is bound by Chapter II has the right to file a demand for international preliminary examination.

REMINDER REGARDING ENTRY INTO THE NATIONAL PHASE (Article 22 or 39(1))

If the applicant wishes to proceed with the international application in the **national phase**, he must, within 20 months or 30 months, or later in some Offices, perform the acts referred to therein before each designated or elected Office.

For further important information on the time limits and acts to be performed for entering the national phase, see the Annex to Form PCT/IB/301 (Notification of Receipt of Record Copy) and Volume II of the PCT Applicant's Guide.

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No. (41-22) 740.14.35

Authorized officer
J. Zahra

Telephone No. (41-22) 338.83.38

PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION CONCERNING SUBMISSION OR TRANSMITTAL OF PRIORITY DOCUMENT

(PCT Administrative Instructions, Section 411)

To:

MANDRAGOURAS, Amy, E.
Lahive & Cockfield, LLP
28 State Street
Boston, MA 02109
ÉTATS-UNIS D'AMÉRIQUE

Date of mailing (day/month/year) 23 December 1999 (23.12.99)	
Applicant's or agent's file reference DFN-031PC	**IMPORTANT NOTIFICATION**
International application No. PCT/US99/25439	International filing date (day/month/year) 29 October 1999 (29.10.99)
International publication date (day/month/year) Not yet published	Priority date (day/month/year) 29 October 1998 (29.10.98)
Applicant DANA-FARBER CANCER INSTITUTE et al	

1. The applicant is hereby notified of the date of receipt (except where the letters "NR" appear in the right-hand column) by the International Bureau of the priority document(s) relating to the earlier application(s) indicated below. Unless otherwise indicated by an asterisk appearing next to a date of receipt, or by the letters "NR", in the right-hand column, the priority document concerned was submitted or transmitted to the International Bureau in compliance with Rule 17.1(a) or (b).

2. This updates and replaces any previously issued notification concerning submission or transmittal of priority documents.

3. An **asterisk(*)** appearing next to a date of receipt, in the right-hand column, denotes a priority document submitted or transmitted to the International Bureau but not in compliance with Rule 17.1(a) or (b). In such a case, **the attention of the applicant is directed** to Rule 17.1(c) which provides that no designated Office may disregard the priority claim concerned before giving the applicant an opportunity, upon entry into the national phase, to furnish the priority document within a time limit which is reasonable under the circumstances.

4. The **letters "NR"** appearing in the right-hand column denote a priority document which was not received by the International Bureau or which the applicant did not request the receiving Office to prepare and transmit to the International Bureau, as provided by Rule 17.1(a) or (b), respectively. In such a case, **the attention of the applicant is directed** to Rule 17.1(c) which provides that no designated Office may disregard the priority claim concerned before giving the applicant an opportunity, upon entry into the national phase, to furnish the priority document within a time limit which is reasonable under the circumstances.

Priority date	Priority application No.	Country or regional Office or PCT receiving Office	Date of receipt of priority document
29 Octo 1998 (29.10.98)	60/106,383	US	21 Dece 1999 (21.12.99)
30 Octo 1998 (30.10.98)	60/106,448	US	21 Dece 1999 (21.12.99)

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LAHIVE & COCKFIELD
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JAN 12 2000
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The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

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